

**REMARKS****Status of the Claims**

Claims 1-3 and 5-24 are pending in the application. Claims 1-3 and 5-24 stand rejected. Claims 1-2, 7, 9-10, 12, 15-17, and 19 are amended herein.

**Claim Rejections****35 U.S.C. § 112, ¶1**

Claims 1-3, 5-14, and 24 stand rejected under § 112, first paragraph, for failing to comply with the written description requirement.

Specifically, the Examiner argues that the phrase “without separation of said red blood cells from said extracellular heme-colored blood substitute prior to analysis” in claims 1 and 9 is not supported by the specification and therefore constitutes new matter. While Applicant respectfully disagrees and asserts that this phrase is fully supported for the reasons of record, the claims have been amended to recite “to measure intracellular hemoglobin concentration and exogenous heme-colored blood substitute concentration in the presence of one another.” Support for this amendment may be found throughout the specification, and in particular at paragraph [0034]. In view of this amendment, Applicant respectfully submits that the rejections under § 112, first paragraph, are overcome.

**35 U.S.C. § 112, ¶2**

The Examiner has rejected claims 1-3, 5-14 and 24 under § 112, second paragraph, arguing that the claim language “said blood sample on an automated cell-by-cell hematology analyzer without separation of said red blood cells from said extracellular heme-colored blood substitute prior to analysis” is unclear. This phrase has been deleted herein. Accordingly, this rejection is overcome.

**35 U.S.C. § 103**

The Examiner has rejected claims 1-3 and 5-24 as being unpatentable over Chupp et al. (US 5,631,165) in view of Chang et al. (US 5,200,323), Samsouondar (WO 98/39634) and Rodriguez et al. (US 6,228,652).

Applicant is puzzled by this continued rejection because none of the cited references teach or remotely suggest measuring intracellular hemoglobin (i.e., hemoglobin inside a red blood cell) in the presence of extracellular heme-colored blood substitutes. In fact, not a single reference cited by the Examiner is concerned with measuring the hemoglobin concentrations in blood samples having both intracellular hemoglobin and extracellular heme-colored blood substitutes.

The present claims each require analyzing a sample on a cell-by-cell hematology analyzer “to measure intracellular hemoglobin concentration and exogenous heme-colored blood substitute concentration in the presence of one another.” None of the cited references, alone or in combination, disclose , suggest, or enable the practice of such a method.

In Chupp, hemoglobin is measured **after the red blood cells are lysed**. The skilled artisan would understand that after the red blood cells are lysed, the intracellular hemoglobin loses its identity as such (because it is no longer inside a cell) and becomes indistinguishable from hemoglobin which was extracellular prior to lysis. Thus, even assuming one were motivated to add heme-colored blood substitutes to the samples of Chupp, there is no teaching whatever in Chupp which would allow one to “measure intracellular hemoglobin concentration and exogenous heme-colored blood substitute concentration in the presence of one another.” Moreover, Chupp does not disclose a sample comprising both intracellular hemoglobin and extracellular heme-colored blood substitute.

In Chang, a whole blood sample is taken from the patient and **the red cells removed to make a plasma sample**. The blood substitute is then added to the plasma sample to test if complement is activated. Thus, Chang does not disclose a sample comprising both intracellular hemoglobin and extracellular heme-colored blood substitute, nor does it remotely suggest a method for determining the concentration of one in the presence of the other.

Samsoondar discloses a method whereby the concentration of a blood substitute in a serum or plasma specimen is identified and quantified. Such plasma samples lack cellular hemoglobin because **the red cells have been removed**. Thus, Samsoondar cannot be said to fairly suggest measuring “intracellular hemoglobin concentration and exogenous heme-colored blood substitute concentration in the presence of one another.”

Rodriguez discloses an analyzer for measuring “erythrocyte cell-by-cell hemoglobin” but does not disclose sample comprising extracellular heme-colored blood substitutes or a method of measuring the same. In sum, Rodriguez does not teach, suggest, or enable the measurement of “intracellular hemoglobin concentration and exogenous heme-colored blood substitute concentration in the presence of one another.”

At most, the combination of these references teach that: (1) intracellular hemoglobin can be measured on a cell-by-cell basis (Rodriguez) or by lysing red blood cells (Chupp); (2) blood substitutes may be added to plasma or serum devoid of red blood cells and consequently devoid of intracellular hemoglobin (Chang); and (3) samples of plasma or serum containing blood substitutes but devoid of red blood cells and consequently devoid of intracellular hemoglobin can be measured. In other words, these references teach that intracellular hemoglobin and blood substitutes can be measured **separately**. However, there is no teaching of preparing a sample comprising both intracellular hemoglobin and blood

substitutes, and certainly no teaching or suggestion of measuring each **in the presence of one another**.

The Examiner has not pointed to any specific motivation in the prior art that would lead the skilled artisan to make the suggested combination and have a reasonable expectation that the combination would be successful. The Examiner appears to be relying on an impermissible hindsight to reconstruct Applicant's invention. Without the knowledge that it is possible to measure intracellular hemoglobin and exogenous heme-colored blood substitute in the presence of one another on a cell-by-cell analyzer -- as provided only by the instant specification -- there simply would have been no motivation to make the suggested combination.

For at least the foregoing reasons, Applicant respectfully requests withdrawal of all rejections under 35 U.S.C. § 103.

Applicant asserts that the foregoing amendments and remarks place the application in condition for allowance and request that these amendments be entered in the record and after due consideration a notice of allowance issued.

#### **AUTHORIZATION**

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **13-4500**, Order No. 0708-4057.

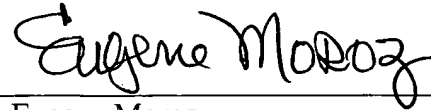
In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is

hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **13-4500**, Order No. 0708-4057.

Respectfully submitted,  
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